REMARKS

It is respectfully requested that this application be reconsidered in view of the following remarks and that all of the claims remaining be allowed.

Rejection Under 35 U.S.C. §102

A. The rejection of claims 1, 4 and 6-10 under 35 U.S.C. §102 as allegedly unpatentable in view of Lee et al. (WO 99/08692) is respectfully traversed for the reasons set forth below.

The standard of anticipation under 35 U.S.C. §102 is that each and every element of the claim must be found in the cited reference. *In re Marshall*, 198 USPQ 344 (CCPA 1978).

Claim 1, the only independent claim, is directed to a method of determining susceptibility of a cell to reovirus infection by measuring constitutive ras-MAP signaling in said cell, wherein the presence of said constitutive signaling indicates susceptibility to infection by reovirus. The phrase "constitutive ras-MAP signaling" means activation of MAP kinase even in the absence of a mitogen, such as serum. For example, the specification discloses:

> Constitutive ras-MAP signaling results in activation of the MAP kinase whether there is a mitogen or not, and activation of the MAP kinase leads to phosphorylation of MAP kinase. (page 10, lines 11-13)
>
> To determine if the Ras pathway was indeed activated in these cell lines, the level of MAPK phosphorylation was assessed in the presence and absence of serum. Those cell lines that were infectable exhibited constitutive MAPK phosphorylation even in the absence of mitogen, while the cell line which was not susceptible to reovirus infection displayed MAPK phosphorylation only in the presence of serum. Therefore, constitutive MAPK phosphorylation is an indication of susceptibility to reovirus infection. (page 15, lines 14-20)
>
> In the diagnostic methods of the invention, the level of MAPK phosphorylation of proliferating cells is determined in the presence or absence of mitogen. The presence of such constitutive ras-MAP signaling in the cells is indicative of susceptibility to reovirus infection. (page 18, lines 1-4)

Lee et al. do not teach measuring ras-MAP signaling in the absence of mitogen or serum. Although Lee et al. describe comparing the ERK1/2 activity of untransformed cells to that of

ras-transformed cells (page 18, second paragraph), there is no indication that the cells were cultured in the absence of serum. In fact, the reference generally teaches that all cell lines were grown in a medium containing 10% fetal bovine serum (page 10, lines 13-14 and page 28, lines 2-3). Although the NIH-3T3 tet-myc cells were cultured in DMEM containing 10% heat-inactivated FBS (page 10, lines 15-18), these cells were not used in the MAP kinase assay. Therefore, the reference does not teach measuring ras-MAP signaling in the absence of mitogen or serum. The reference also does not teach that constitutive signaling indicates susceptibility to infection by reovirus.

Accordingly, Lee et al. do not teach each and every element of the claimed invention, and withdrawal of this rejection is respectfully requested.

B. The rejection of claims 1, 4 and 6-10 under 35 U.S.C. §102 as allegedly unpatentable in view of Strong et al. (EMBO J. 17(12):3351-3362, 1998) is respectfully traversed for the same reasons as discussed above. Strong et al., like Lee et al., compared the ERK1/2 activity of untransformed cells to that of ras-transformed cells (page 3354, left column). However, Strong et al. do not teach the measurement of constitutive MAP kinase activation, or that the cells for this assay should be kept in the absence of serum or mitogen. The Materials and Methods section discloses that the cells were generally grown in a medium containing 10% fetal bovine serum (page 3360, left column). Although the NIH-3T3 tet-myc cells were cultured in DMEM containing 10% heat-inactivated FBS (*Id.*), these cells were not used in the MAP kinase assay. Accordingly, the reference does not teach measuring ras-MAP signaling in the absence of mitogen or serum, or that constitutive signaling indicates susceptibility to infection by reovirus.

Therefore, Strong et al. do not teach each and every element of the claimed invention, and withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. §103

The rejection of claims 1-4 and 6-10 under 35 U.S.C. §103 as allegedly unpatentable over Lee et al. and Strong et al. (as applied to claims 1, 4 and 6-10 above), and further in view of

Nguyen et al. (J. Bio. Chem. 146(1):149-164, 1999), is respectfully traversed for the reasons set forth below.

To properly issue a rejection under 35 U.S.C. §103, the USPTO bears the initial burden to establish a *prima facie* case of obviousness by meeting three criteria. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to arrive at the claimed invention. *In re Vaeck*, 20 USPQ 2d 1438 (Fed. Cir. 1991). Second, there must be a reasonable expectation of success. *Id.* Finally, the prior art reference or the combination of references must teach or suggest all the claim limitations. *In re Royka*, 180 USPQ 580 (CCPA 1974).

This rejection does not meet these criteria. As discussed above, neither Lee et al. nor Strong et al. teach or suggest measuring ras-MAP signaling in the absence of mitogen or serum, or that constitutive signaling indicates susceptibility to infection by reovirus. Since Nguyen et al. do not cure this deficiency, the combination of references does not teach or suggest all the required claim elements. The combined references also do not offer any motivation or suggestion that ras-MAP signaling should be measured in the absence of mitogen or serum to determine reovirus susceptibility. Furthermore, the references, either alone or in combination, do not provide a reasonable expectation that constitutive ras-MAP signaling indicates susceptibility to infection by reovirus. Therefore, the requirement under 35 U.S.C. §103 is not satisfied.

Accordingly, withdrawal of this rejection is respectfully requested.

Conclusions

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 839-5044.

Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: Nov. 23, 2005

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